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Neural Modeling of Motor Cortex and Spinal Cord

The general goal of this research was to model the translation of motor cortical commands for movements in space to motoneuronal output through an intercalated system of intercalated interneurons.

The specific objectives were:

1. To develop a physiologically relevant, neural network to model time-varying neuronal population operations in the motor cortex, dealing with movements in space;

2. To develop a model of interactions between the cortical and the spinal networks dealing with generating time-varying motoneuronal outputs for movements in space.

The novelty of our approach consisted in:

(a) The realistic nature of the elements in our networks;
(b) The massive and asymmetric interconnectivity among network elements;
(c) The physiologically relevant design of the networks, including the communication by spike trains among network elements and rules of connectivity based on experimental findings;
(d) The dynamical behavior of the networks; and
(e) The time-varying performance of the networks.

Results and Discussion

1. **Development of a physiologically relevant, neural network to model time-varying neuronal population operations in the motor cortex, dealing with movements in space (publications 1-6;** numbers in parentheses refer to the list of papers in which the work was published, whereas named quotations refer to the Literature Cited).

We published 7 papers on this work. We summarize below the main findings with respect to (A) a network using simple input-output neurons, (B) a network using biophysically modeled, spiking neurons, and (C) a model of interacting neural networks.

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We developed physiologically relevant, neural networks to model time-varying neuronal population operations in the motor cortex and spinal cord, dealing with movements in space. We also developed a model of the interactions between these two networks dealing with generating time-varying motoneuronal outputs for movements in space. The novelty of our approach consisted in (a) the realistic nature of the elements in our networks, (b) the massive and asymmetric interconnectivity among network elements, (c) the physiologically relevant design of the networks, including the communication by spike trains among network elements and rules of connectivity based on experimental findings, (d) the dynamical behavior of the networks, and (e) the time-varying performance of the networks. Finally, we were able to reliably decode and transform the neuronal ensemble activity recorded in behaving animals for controlling an simulated arm. This demonstration suggests that the use of biologically inspired neural networks to transform raw cortical signals into the motor output of a multijoint artificial limb is both feasible and practical time-varying performance of the networks.

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1.A. Motor cortical network using simple input-output neurons

Abstract

As a dynamical model for motor cortical activity during hand movement we constructed an artificial neural network that consists of extensively interconnected neuron-like units and performs the neuronal population vector operations. Local geometrical parameters of a desired curve are introduced into the network as an external input. The output of the model is a time-dependent direction and length of the neuronal population vector which is calculated as a sum of the activity of directionally tuned neurons in the ensemble. The main feature of the model is that dynamical behavior of the neuronal population vector is the result of connections between directionally tuned neurons rather than being imposed externally. The dynamics is governed by a system of coupled non-linear differential equations. Connections between neurons are assigned in the simplest and most common way so as to fulfill basic requirements stemming from experimental findings concerning the directional tuning of individual neurons and the stabilization of the neuronal population vector, as well as from previous theoretical studies. The dynamical behavior of the model reveals a close similarity with the experimentally observed dynamics of the neuronal population vector. Specifically, in the framework of the model it is possible to describe a geometrical curve in terms of the time series of the population vector. A correlation between the dynamical behavior of the direction and the length of the population vector entails a dependence of the "neural velocity" on the curvature of the tracing trajectory that corresponds well to the experimentally measured covariation between tangential velocity and curvature in drawing tasks.

Introduction

Although individual neurons in the motor cortex are broadly tuned with respect to the direction of movement (Georgopoulos et al. 1982) and a particular direction involves the activation of a large ensemble of cells, the high accuracy of a movement performance can be explained by means of "population coding" hypothesis (Georgopoulos et al. 1983; Georgopoulos et al. 1986; Georgopoulos et al. 1988). In this hypothesis the contribution of each i^{th} directionally tuned neuron is represented as a vector pointing in its preferred direction $\boldsymbol{C}_i$ with the length given by the change in cell frequency of discharge associated with a particular movement direction. For a given movement $\boldsymbol{M}$, these contributions add vectorially to yield the "neuronal population vector" $\boldsymbol{P}$, which is a measure of the combined directional tendency of the whole neuronal ensemble:

$$P(M;t) = \sum_i V_i(M;t)\, C_i \qquad (1)$$

where $V_i(\boldsymbol{M};t)$ is the activity of the i^{th} neuron at time bin t (usually 10-ms or 20-ms bin). Now it is well-established that the neuronal population vector predicts accurately the direction of

movement under a variety of conditions (Georgopoulos 1990).

Remarkably, the population vector can be used as a probe to monitor the directional tendency of the neuronal ensemble, as it changes in time. For example, in a task that required a movement to be made at a given angle from a stimulus direction, the population vector rotated from the stimulus direction to the direction of the movement (Georgopoulos et al. 1989; Lurito et al. 1991). Moreover the "neural trajectories" reconstructed from the time series of neuronal population vectors attached to each other tip-to-tail correspond well to the actual movement trajectories produced in reaching (Georgopoulos et al. 1988) as well as in drawing tasks (Schwartz 1993, 1994). All of these findings indicate that the ongoing direction and length of the neuronal population vector could predict the tangential velocity vector of the movement that is made approximately 120 ms later (Schwartz 1993). In its turn, a stable covariation between the tangential velocity of the hand movement and the curvature of a drawn trajectory has been well documented (Viviani and Terzuolo 1982; Lacquaniti et al. 1983; Soechting and Terzuolo 1986; Massey et al. 1992). Qualitatively, this correlation reflects the fact that the movement tends to slow down when the trajectory is more curved. It was hypothesized (Massey et al. 1992) that the underlying mechanisms of the covariation between geometrical and kinematic parameters of the movement could be neural constraints. Namely, if indeed the neuronal population vector predicts the tangential velocity vector of the real movement, then the reason of the tendency to slow down at the curved sections of a trajectory could be explained by the additional time, compared with straight-line movement, needed for the rotation of the neuronal population vector. However, the neural basis which would explain qualitative and quantitative aspects of the problem remains to be explored.

The distributed coding of the direction of movement as well as stationary properties of the ensemble of motor cortical units have been well reproduced in the framework of simple three-layered model trained through a supervised learning algorithm (Lukashin 1990), by means of the model of arrays of adjustable pattern generators (Berthier et al. 1991) and within a more biological model that computes visuomotor transformations for arm reaching movements (Burnod et al. 1992). The purpose of this paper is to propose a simple *dynamical* neural network model which consists of extensively interconnected neuron-like units and performs the neuronal population vector operations as a response to some input information. Specifically, we consider a model of neural network which receives the input in terms of geometrical features of a trajectory and produces the dynamical behavior of the neuronal population vector as the output. The dynamical properties of the neuronal population vector as well as a relation between the curvature of a trajectory and tangential velocity obtained in the framework of the model reveal close correspondence with the experimental findings mentioned above.

Model

Basic requirements. Generally, the present model belongs to a well-known class of neural networks which are able to generate sequential patterns of neural activity (Kleinfeld 1986; Sompolinsky and Kanter 1986; Jordan 1986; Dehaene et al. 1987; Kleinfeld and Sompolinsky 1988; Guyon et al. 1988; Schoner and Kelso 1988; Massone and Bizzi 1989; Williams and Zipser 1989; Pearlmutter 1989; Amirikian and Lukashin 1992). Therefore below we will

concentrate only on those features of the model that are essential for the problem in question.

Let K_x and K_y be the x and y components of a unit length tangential vector $\boldsymbol{K}$ taken at a point K on drawn trajectory. Let M_x and M_y be the same values for a subsequent point M. Receiving components of the vectors $\boldsymbol{K}$ and $\boldsymbol{M}$ as external input, the desired network has to produce components of the neuronal population vector $\boldsymbol{P}$ as a sum of the responses of the ensemble directionally tuned neurons [see (1)]. The basic qualitative requirements for the dynamical behavior of the neuronal population vector follow from experimental findings concerning the dynamical behavior of the neuronal population vector during a transformation task (Georgopoulos et al. 1989; Lurito et al. 1991). The observed dynamical behavior of the neuronal population vector in the case with externally assigned initial (stimulus) and final (movement) directions consists of the rotation of the population vector from an initial to a final direction, followed by the stabilization of the direction and the length of the population vector. Hence we suppose that at the motor cortical level the tracing out the section of a trajectory between point K with tangential vector $\boldsymbol{K}$ and point M with tangential vector $\boldsymbol{M}$ corresponds to the rotation of the neuronal population vector $\boldsymbol{P}$ from the direction $\boldsymbol{K}$ to the direction $\boldsymbol{M}$ with subsequent stabilization in the direction $\boldsymbol{M}$. The stabilization of the direction of the population vector triggers the change of the external signals: now the direction $\boldsymbol{M}$ is considered by the network as the initial direction and a new final desired direction (for example, tangential vector $\boldsymbol{N}$ of the next point N on the trajectory) is given as a new external input. This assumption is conceptually in accord with the mechanisms of continuous updating of the current position commands to arm system muscles, introduced by Bullock and Grossberg (1988) in a model of the circuit that automatically generates arm movement trajectories.

Architecture. The input (upper) layer of the network consists of four neurons the activities of which code components of vectors $\boldsymbol{K}$ and $\boldsymbol{M}$. Only the activities of these neurons are assigned externally. The output (lowest) layer consists of two neurons with linear activation functions. The activities of these neurons are supposed to code components of the neuronal population vector $\boldsymbol{P}$. There are two hidden layers in the network: a layer of modulators whose activities are designated by Q (only one of them is shown) and a layer of directionally tuned neurons whose activities are designated by V_i, where index i enumerates neurons in the layer. The activities of all neurons in both hidden layers are determined by a nonlinear activation function which is chosen as hyperbolic tangent function.

There are connections v_{ix}, v_{iy} between neurons K_x, K_y of the input layer, which code the initial direction $\boldsymbol{K}$, and all neurons V_i of directionally tuned hidden layer. Correspondingly, there are connections w_{xi}, w_{yi} between all V_i neurons and the two neurons P_x, P_y in the output layer. The essential feature of the model is the existence of intralayer connections between neurons V_i in the directionally tuned layer. These connections are of two types: modulated, v_{ij}, and non-modulated, w_{ij} (see below). The modulator neuron Q receives inputs from neurons M_x, M_y, which code the required final direction $\boldsymbol{M}$, and, by means of feedback connections, from the two neurons P_x, P_y of the output layer, which code the current direction of the neuronal population vector. For the sake of simplicity the absolute values of all these connections are supposed to have the same strength q^{inp}. The modulator neuron Q sends signals to directionally tuned neurons V_i in a way that the efficacy of modulated connections v_{ij} between neurons V_i and the efficacy of connections v_{ix}, v_{iy} between neurons V_i and neurons K_x, K_y depend on the activity of modulator Q and on the connection strengths between neuron Q and neurons V_i. Again the latter connections are

supposed to have the same strength q^{out}.

Dynamical equations. In the framework of standard theory of neural networks (see, for instance, Amari 1972; Sejnowski 1976; Grossberg and Cohen 1983; Hopfield 1984; Hopfield and Tank 1986; Atiya and Baldi 1989) the dynamical behavior of the model described above is governed by the following system of coupled nonlinear differential equations:

$$\tau \frac{d u_i}{dt} = - u_i(t) + \sum_j w_{ij} V_j(t) + \left(\sum_j v_{ij} V_j(t) + v_{ix} K_x + v_{iy} K_y \right) q^{out} Q(t) \qquad (2)$$

$$V_i(t) = \tanh(u_i(t)) \qquad (3)$$

$$P_x(t) = \sum_i w_{xi} V_i(t); \qquad P_y(t) = \sum_i w_{yi} V_i(t) \qquad (4)$$

$$Q(t) = \tanh\left[q^{inp} \left(|M_x - \tilde{P}_x(t)| + |M_y - \tilde{P}_y(t)| \right) \right] \qquad (5)$$

Argument t is shown for variables which depend on time. Equation (2) is a resistance-capacitance equation for the i^{th} neuron of the directionally tuned layer (variable u_i, for example, might represent the soma membrane potential of the neuron averaged over a reasonable time interval). The time constant $\hat{o}$ is a characteristic time for the individual neuron. To simplify the equations, characteristic times for neurons in other layers are supposed to be much shorter then the $\hat{o}$ value. We checked that this approximation does not change the main results presented below. Equation (3) shows the relation between internal state of the i^{th} neuron and its output activity V_i (this value might correspond to the change of discharge rate of a real cell averaged over a reasonable time interval). In accordance with the model, the activity of the modulator Q at time t (5) is the function of the components of the constant vector $\boldsymbol{M}$ and the components of vector $\boldsymbol{P}$ at time t. [Tilde above means that vector $\boldsymbol{P}$ is normalized to unity in (4)]. The components of vector $\boldsymbol{P}$ are linear functions of activities $V_i(t)$, as can be seen from (4).

Once equations (2)-(5) are written, the dynamical behavior of the model completely depends on the set of connection strengths. In the next section we explain the motivation for our choice of these parameters.

Connection strengths

Directional tuning of neurons. Suppose that there are no intralayer connections between neurons V_i (or $w_{ij} = 0$, $v_{ij} = 0$) and no feedback connections to modulator ($Q(t)$. 1). Then equations (2) are reduced to ordinary differential equations having straightforward solution, which for t o $\hat{o}$ and q^{out} n 1 leads to the relations:

$$V_i(t \ll \tau) \approx q^{out}\left(v_{ix} K_x + v_{iy} K_y\right) = q^{out} k_i \cos(\theta_K - \alpha_i) \qquad (6)$$

where è$_K$ is the angle characterizing the direction of the input vector $\boldsymbol{K}$, and parameters k_i and á$_i$ are expressed through connection strengths v_{ix}, v_{iy}. Since (6) gives the same response activity to the external direction $\boldsymbol{K}$ as has been observed in numerous experiments (Georgopoulos et al. 1982; Schwartz et al. 1988; Schwartz 1992) the angle á$_i$ can be regarded as the *preferred direction* of the i^{th} neuron. The important property of the real ensemble of directionally tuned neurons is the uniform distribution of preferred directions in space (Schwartz et al. 1988; Burnod et al. 1992). The same type of distribution was obtained in the framework of the simplified model (without intralayer connections) by means of adjusting the set of the v_{ix}, v_{iy} parameters through a supervised learning algorithm (Lukashin 1990). In accordance with these results, we use for the complete model (2)-(5) the following expressions for connection strengths [compare with (6)]:

$$v_{ix} = \cos\alpha_i; \qquad v_{iy} = \sin\alpha_i \qquad (7)$$

where angles á$_i$ are randomly and uniformly distributed over the interval [-ð,ð]. Since the preferred directions are given, connection strengths w_{xi}, w_{yi} (see (4)) should lead to the standard definition of the neuronal population vector (1). Namely,

$$w_{xi} = \frac{2}{N}\cos\alpha_i; \qquad w_{yi} = \frac{2}{N}\sin\alpha_i \qquad (8)$$

where ($2/N$) is a normalizing coefficient, N is the number of neurons in the directionally tuned layer. Equations (8),(4) are completely equivalent to (1).

Stabilization of the neuronal population vector. Suppose that the direction of the neuronal population vector $\boldsymbol{P}$ is close enough to the desired final direction $\boldsymbol{M}$, or $Q(t)$. 0 [see (4)]. Then only the first and second terms in the right-hand side of (2) are retained. In accordance with experimental findings in this case (Georgopoulos et al. 1989; Lurito et al. 1991), the direction of the neuronal population vector should be stable. During this steady-state period activities of directionally neurons cease to change, so that $du_i/dt = 0$ for all i, which together with (2) and (3)

leads to the condition

$$V_i(\mathrm{M}) = \tanh\left(\sum_j w_{ij} V_j(\mathrm{M})\right) \qquad (9)$$

that should be valid for all neurons and, generally, for all directions ***M***. If activities V_i at the stable state are known for a given number of neurons and for an appropriate number of directions ***M***, equation (9) can be used for determining the parameters w_{ij}. The general features of the sets of connection strengths w_{ij} that would ensure the stability was extensively studied (Georgopoulos et al. 1993). It was shown that under some restrictions on its possible values, the w_{ij} parameters ensuring condition (9) depend on preferred directions of the pair of neurons involved in the connection. Namely, the mean synaptic strength was negatively correlated with the angle between the preferred directions of the two neurons throughout the range of connections, from positive (excitation) to negative (inhibition). These results of modeling were confirmed by the findings of neurophysiological studies [for details see (Georgopoulos et al. 1993)]. The simplest way to include the dependence on preferred directions is to approximate the w_{ij} parameters by a cosine relation:

$$w_{ij} = \frac{2}{\mathrm{N}} \cos(\alpha_i - \alpha_j) \qquad (10)$$

However we checked that sets of the parameters w_{ij} obtained in (Georgopoulos et al. 1993) lead to the same results as the set (10).

Rotation of the neuronal population vector. The dynamical behavior of the system producing the rotation of the neuronal population vector can be ensured by connections that induce the phase shift violating steady-state conditions. Again the simplest way to include this phase shift is to assign modulated intralayer connection strengths v_{ij} by the relations:

$$v_{ij} = \frac{2}{\mathrm{N}} \sin(\alpha_i - \alpha_j), \quad (i \_ j) \qquad (11)$$

To allow for the possibility of changing the length of the population vector we introduce a self-inhibition for activities of neurons in the directionally tuned layer (non-zero negative values of the diagonal elements v_{ii}). The self-inhibition is under control by the feedback loop in the same way as it is realized for the modulator Q.

Results of simulations and discussion

Below we give the results of calculations of the dynamical behavior of the model described by (2)-(5) with connection strengths given by (7),(8),(10),(11). Preferred directions á$_i$ are randomly and uniformly distributed over the interval [-ð,ð]. The number of neurons in directionally tuned layer in routine calculations is $N = 100$.

Adjustable parameters. Only three adjustable parameters remain to be established: the characteristic time $\hat{o}$ (2), the input, q^{inp}, and the output, q^{out}, connections of the modulator [see (2),(5)]. The parameter $\hat{o}$ determines the time scale of the dynamics. A reasonable value is $\hat{o}$. 5 ms. We checked that the results do not depend on a particular value of the q^{inp} parameter if it is large enough. (All the results presented below have been obtained for $q^{inp} = 50$.) In contrast, the model reveals a strong sensitivity to the value of the q^{out} parameter. The chosen set of connection strengths provides dynamics such as a movement towards an attractor. It can be seen that the population vector rotates from the direction of vector $\boldsymbol{K}$ towards the direction of vector $\boldsymbol{M}$ and then stabilizes in the latter direction. The shape of the curves as well as the saturation level essentially depends on the value of the q^{out} parameter. It makes sense to adjust this parameter so as to obtain the angular velocity of rotation at initial moments of time close to the experimentally measured value which is of the order of 500 deg/s (Georgopoulos et al. 1989; Lurito et al. 1991). From this point of view the curve corresponding to $q^{out} = 0.05$ gives the best fit. Indeed, in this case the angular velocity is around 2.5 deg per $\hat{o}$ unit or 500 deg/s, if $\hat{o}$. 5 ms. All the results shown below were obtained for $q^{out} = 0.05$.

Feedback connections. In the beginning of the dynamics, when the current direction of population vector is far enough from the desired final direction, the population vector rotates with constant angular velocity. When the direction of population vector becomes close to the assigned final direction $\boldsymbol{M}$, the activity of the modulator Q tends to zero. The third term in the right-hand side of the basic equation (2) ceases to affect the dynamics, and the process enters into the steady-state phase. The stabilized directions of the population vector coincide with the directions of vectors $\boldsymbol{M}$. In the light of experimental data concerning the dynamical behavior of population vector during a transformation task (Georgopoulos et al. 1989) we consider the steady-state phase as the necessary part of the whole dynamics.

Population coding of movement trajectories. The aim of this section is to check the ability of the model to describe trajectories in terms of time series of the neuronal population vectors attached to each other tip-to-tail if the geometrical features of a trajectory are introduced into the network as external input. Here, as an example, we consider closed elliptic trajectories. We checked that all the results remain valid for other curves.

Let a desired trajectory be given. Let K, M, N,... be points along the trajectory separated from each other by equal arc lengths (in routine calculations we used 100 points per each trajectory). The beginning of the dynamics is considered to be the instant at which the components of first two tangential vectors $\boldsymbol{K}$ (initial) and $\boldsymbol{M}$ (final) are introduced into the network as activities of corresponding neurons. Then the dynamics described by (2)-(5),(7),(8),(10),(11) begins. When the current direction of population vector $\boldsymbol{P}$ becomes close to the direction $\boldsymbol{M}$ the activity of the modulator Q rapidly tends to zero. On the one hand, this entails the stabilization of the population vector $\boldsymbol{P}$. On the other hand, the low value of the activity of the modulator Q triggers the change of the input signals. Now vector $\boldsymbol{M}$ serves as the initial direction, and the next tangential vector $\boldsymbol{N}$ is introduced as a desired final direction, and so on. It is important to note

that in the framework of this procedure the relative velocity of tracing of the trajectory is determined by the network itself because the instant of appearance of the next input signal depends only on the internal state of the network.

Conclusion

The main feature of the proposed model is that the neuronal population vector operations produced by the network are the result of the interactions between directionally tuned neurons rather than being imposed by external inputs. Connections between neurons were assigned in the simplest and most common way so that actually only one numerical parameter, namely q^{out}, has been adjusted. The network receives inputs as a sequence of tangential vectors of a curve which is to be traced out, but the "neural velocity" of the tracing is a function of internal parameters of the model. The output of the network is the current direction and length of the population vector. The correspondence between the changes of these parameters during tracing a trajectory makes it possible to describe a drawn geometrical curve in terms of the time series of the population vector in full agreement with experimental findings (Georgopoulos et al. 1988; Schwartz 1993, 1994). Moreover, the dependence of the "neural velocity" on the curvature obtained in the framework of the model reveals close correspondence with the similar covariation observed experimentally for hand movement in drawing tasks (Viviani and Terzuolo 1982; Lacquaniti et al. 1983; Soechting and Terzuolo 1986; Massey et al. 1992).

The network considered in this paper possesses three major characteristics that are biologically relevant for cortical operations in general and two properties that are important for the motor cortex in particular. The general characteristics include the massive interconnectivity among the network elements, the weak strength of synaptic connections and the correlated interactions: indeed, these seems to be general features of cortical processing (Martin 1988). The specific properties of the network that correspond to motor cortical operations include the directional tuning of individual elements and the computation of the neuronal population vector. Altogether then, this network combines biologically meaningful aspects which are embedded within a dynamical behavior that evolves in time. This temporal evolution combines an experimentally observed operation (i.e. the rotation of the neuronal population vector) and applies it to the neural representation of curvature in a planned movement trajectory. However, for this application an internal feedback mechanism is proposed that signals the completion of a unit rotation; this hypothesized feedback mechanism needs to be identified experimentally. It is this interplay between theory and experiment that lies in the heart of the present attempt to bridge artificial and real neural networks within the domain of the motor cortex.

1.B. Motor cortical network using biophysically modeled, spiking neurons

Abstract

A biophysically realistic neural network is presented that models operations in an ensemble of directionally tuned neurons in the motor cortex. The model reproduces well directional operations previously identified experimentally, including the prediction of the direction of an

upcoming movement in reaching tasks and the rotation of the neuronal population vector in a directional transformation task.

Introduction

The model described in the previous section consisted of formal, input-output neurons. In this work we describe a biologically relevant model neural network that models the motor cortical activity during the intended movement in the framework of the second hypothesis above. The key idea is that a correlation between synaptic connection strengths and preferred directions of the neurons involved in the connection could ensure the observed stability and transformations of the neuronal population vector. We showed previously (Georgopoulos et al. 1993) that this holds for a formal neural network; in this paper we extend this work to a realistically modeled, spiking neural network.

Model

Although simulations of the dynamical behavior of the neuronal population vector by modeling neurons as simple input-output devices were carried out (Lukashin 1990; Lukashin and Georgopoulos 1993), it is still unclear where is the border between important features and incidental details in the modeling of motor cortical cells. Hence, more realistic models are desirable. In the present paper we simulate an artificial network that consists of 48 heavily interconnected directionally tuned neurons modeled at a reasonable level of reality. Real motor cortical neurons produce trains of action potentials, or spikes, and it is the timing of these spikes that carries information about the directional tendency. At the same time, for the problem in question it is obviously premature to allow for details concerning, for example, spatial localization of channels or dendritic branching patterns.

To describe a neuron and interactions between cells we use a biophysical model of intermediate complexity. A neuron is represented as a one-compartment cell equipped with a standard set of active channels with kinetics governed by the Hodgkin-Huxley type equations (Hodgkin and Huxley 1952; Koch and Segev 1989). At present, each cell has voltage-dependent sodium and potassium channels, and a calcium-dependent potassium channel that generates the late-phase afterhyperpolarization. The intracellular level of free calcium is the sum of two calcium currents: the first corresponds to the influx through voltage gated calcium channel, and the second corresponds to calcium that enters through the NMDA channel. The depolarizing current resulting from the influx of calcium ions has been ignored. Specifically, the system of equations listed in (Ekeberg et al. 1991) has been used to calculate the ionic currents, calcium level and corresponding voltage- and time- dependent degrees of activation/inactivation of the channels. The relevant parameters are presented in Table 1. (The 28 parameters were used in describing exponential expressions for the rate constants of activation/inactivation of the channels are exactly the same as those listed in Table 1 of (Ekeberg et al. 1991) and are not shown).

All neurons are connected with each other, and changes in synaptic conductance are used to model conventional excitatory and inhibitory synaptic interactions. A contribution of the synaptic currents into the total current entering a cell is calculated as a liner sum over all

synapses. Ionic current resulting from activation of a synapse due to arriving of a presynaptic action potential is calculated as the product of time-dependent synaptic conductance and the difference between the reversal potential of the synapse and the membrane potential of the cell. The synaptic conductance decreases exponentially with a decay time constant. If another presynaptic spike arrives while a residual synaptic current remains, the conductance is not allowed to increase above the level assigned for a single spike (Ekeberg et al. 1991). The model is capable of producing action potentials with a realistic shape and in a realistic, for the motor cortical cells, firing frequency range between 10 and 70 impulses per second.

To make the model specific to a description of the motor cortical network two additional factors are introduced. First, each i^{th} neuron receives an extra stimulation by intracellular current injection. This extra current, E_i, serves to assign the preferred direction of the neuron. Specific expression for the current E_i is chosen in order to reproduce quantitatively the directional tuning curve, or the changes in motor cortical cell activity related to changes of externally given direction of the movement. The experimentally observed tuning curve can be approximated as a linear function of the cosine of the angle between the preferred direction of a cell and the movement direction (Georgopoulos et al. 1982; Schwartz et al. 1988). Within the model this condition leads to the following relation:

$$E_i = b + a\cos(\theta - \alpha_i) \tag{1}$$

where the angle θ corresponds to externally given direction, the angle α_i is the preferred direction angle of the i^{th} neuron, b and a are adjustable parameters. The observed tuning curves are reproduced if the following values of the parameters are used: $b = 3.0$ nA, $a = 2.2$ nA. Second, the value of synaptic conductance corresponding to the connection between j^{th} (presynaptic) and i^{th} (postsynaptic) neurons shown in Table 1 is multiplied by an additional parameter, the connection strength w_{ij}, and the type of a synapse (excitatory or inhibitory) is determined by the sign of the w_{ij} value (positive or negative correspondingly). A specific form of the correlation between the connection strengths w_{ij} and the preferred direction angles α_i is chosen in accordance with the experimental findings (Georgopoulos et al. 1993). It was shown (Georgopoulos et al. 1993) that weights of functional connections between directionally tuned neurons tend to be negatively correlated with the difference between the preferred directions. A first obvious approach to model this correlation is to represent an unknown function $w_{ij}(\alpha_i-\alpha_j)$ as the sum of two harmonics:

$$w_{ij} = d\cos(\alpha_i - \alpha_j) + c\sin(\alpha_i - \alpha_j) \tag{2}$$

where d and c are adjustable parameters that coordinate relative contribution of symmetric and anti-symmetric components, and $d>0$. The correlation between the weight of the synaptic connection w_{ij} and the angles α_i, α_j is the main feature of the suggested model.

Simulations and discussion

The dynamics of the network is governed by the system of 384 coupled differential equations (8 equations per each neuron). Expressions for the extra currents E_i and for the synaptic connection strengths w_{ij} are described by (2),(3). The preferred direction angles α_i are uniformly distributed on the interval $[-\pi,\pi]$. For a given set of parameters the system of differential equations is solved using fifth-order Runge-Kutta formula.

We found that a directional tendency of the network emerged due to segregation of neurons imposed externally by extra currents E_i (see Fig. 1 in Lukashin and Georgopoulos, 1994). The direction of the population vector coincided with the externally given direction $\theta = 0$ deg. At the instant of time 150 ms the symmetric component of the synaptic connections was switched on, that is, $w_{ij} = \cos(\alpha_i - \alpha_j)$. After this moment the directional tendency becomes even stronger because of an inhibition of the firing of neurons whose preferred direction are far from the externally given direction 0 deg. The most interesting dynamical period begins at 300 ms, when the part of external currents that realized the specification of neurons by their preferred directions [second term in the right-hand side of (1)] was switched off. Starting from this moment, there is no directional influence that would come from outside the network, since all neurons receive the equal extra current $E_i = 3.0$ nA. Nevertheless the directional tendency of the network is being kept through the mechanism of the correlated interactions between cells (see the spike trains and population clusters at the interval 300 - 900 ms). These simulations showed that the experimentally observed stability of the directional tendency of the motor cortex lasting several hundred milliseconds (Georgopoulos et al. 1986; Georgopoulos et al. 1989a; Georgopoulos et al. 1993) could be ensured by specifically correlated synaptic connections between cells even without any directional influence from areas outside the motor cortex. Finally, the ability of the network to reproduce a basic type of transformations of the neuronal population vector, namely its rotation, was also demonstrated. The rotation of the population vector at 90 deg takes approximately 100-150 ms (between 400 and 550 ms), which gives a velocity value of about 600-900 deg/s. This value is quite close to the experimentally measured angular velocity of the rotation of the neuronal population vector which is about 400-700 deg/s (Georgopoulos et al. 1989b; Lurito et al. 1991).

These results demonstrate that the main features of experimentally observed motor cortical activity related to the directional tendency can be reproduced within the suggested model. The following remarks are noteworthy. First, the results are not specific to the model, nor to the set of parameters chosen. We checked the robustness of the results in respect to changes of parameters within a reasonable range, and we obtained qualitatively the same results for a model with simplified channel kinetics close to that one suggested by (Bush and Sejnowski 1991). Second, concerning the assignment of the preferred directions of the neurons, we checked that using external current is not the only way to for this assignment: we obtained the same results by modeling external directional influences by adding extra neurons with correspondingly assigned strengths of the synaptic connections. In the present paper only one particular type of the correlation between the weight of the synaptic connection and the difference between the preferred directions of neuronal pair involved in the connection (3) has been tested. Previous results of a study of the stability problem performed in (Georgopoulos et al. 1993) within a more

simple model show that other types of this solution might be expected. A global change of the synaptic connection strengths that induced within the model the rotation of the population vector might have its biological analog as so-called saliency systems which are able to affect many cortical synapses simultaneously by release of a modulatory neurotransmitter (Harris-Warrick and Marder 1991; Tononi et al. 1992).

Table 1. Parameters used for the simulations.

Parameter	Value
Cell	
Leak current equilibrium potential	-70 mV
Sodium equilibrium potential	50 mV
Potassium equilibrium potential	-90 mV
Calcium equilibrium potential (voltage gated)	150 mV
Calcium equilibrium potential (NMDA gated)	20 mV
Membrane capacitance	0.05 nF
Membrane leak conductance	0.01 μS
Sodium conductance	1.00 μS
Potassium conductance	0.50 μS
Calcium-dependent potassium conductance	0.02 μS
Calcium accumulation rate (voltage gated)	0.0040 $mV^{-1}ms^{-1}$
Calcium accumulation rate (NMDA gated)	0.0005 $mV^{-1}ms^{-1}$
Calcium decay rate (voltage gated)	0.0300 ms^{-1}
Calcium decay rate (NMDA gated)	0.0030 ms^{-1}
Excitatory synapses	
Reversal potential	0 mV
Conductance after spike	$0.003w^*$ μS
Decay time constant	100 ms
Inhibitory synapses	
Reversal potential	-85 mV
Conductance after spike	$0.015w^*$ μS
Decay time constant	20 ms

1.C. A model of interacting networks

Abstract

The hypothesis was tested that learned movement trajectories of different shapes can be stored in, and generated by, largely overlapping neural networks. Indeed, it was possible to train a massively interconnected neural network to generate different shapes of internally stored,

dynamically evolving movement trajectories using a general-purpose, core part, common to all networks, and a special-purpose part, specific for a particular trajectory. The weights of connections between the core units do not carry any information about trajectories. The core network alone could generate externally instructed trajectories but not internally stored ones, for which both the core and the trajectory-specific part were needed. All information about the movements is stored in the weights of connections between the core part and the specialized units and between the specialized units themselves. Due to these connections the core part reveals specific dynamical behavior for a particular trajectory and, as the result, discriminates different tasks. The percentage of trajectory-specific units needed to generate a certain trajectory was small (2-5%), and the total output of the network is almost entirely provided by the core part, whereas the role of the small specialized parts is to drive the dynamical behavior. These results suggest an efficient and effective mechanism for storing learned motor patterns in, and reproducing them by, overlapping neural networks, and are in accord with neurophysiological findings of trajectory-specific cells and with neurological observations of loss of specific motor skills in the presence of otherwise intact motor control .

Introduction

Although a wealth of knowledge has accumulated concerning the neural mechanisms of visually guided reaching (Georgopoulos et al. 1993) and tracing (Schwartz 1993) movements, and the design and performance of artificial neural networks for similar movements (see previous sections), our knowledge concerning the generation and performance from memory of explicitly defined, learned movement trajectories, such as drawing a circle, are largely unknown. Certain brain lesions can result in apparently specific loss of particular motor skills ["apraxia", see De Renzi 1986], such as dressing or buttoning a garment, without affecting other motor skills (e.g driving a car) or simple movements (e.g. reaching to a target). It is generally assumed that information concerning the performance of the lost motor skill is stored in the lesioned areas (commonly in the posterior parietal cortex) or that these areas are unique in triggering the appropriate motor action, the motor pattern of which is stored elsewhere. Whatever the mechanism, the crucial supposition is that the neural pattern of a motor skill [Lashley's "motor engram"] is stored somewhere *in toto* so that, when activated, it unfolds in time as a skilled motor act. Since movements are the result of interactions among neurons in the brain, it is reasonable to hypothesize that the motor engram could be stored in the set of connections and synaptic strengths between interacting neurons within and among various sensorimotor areas. This distributed representation of the motor skill could account for the elusiveness of the nature and the site of its motor engram. The neural networks subserving specific motor engrams could be separate and very specific in their composition and connection strengths, so that a particular learned, skilled action could be generated by the exclusive activation of the corresponding network with a fixed set of connection strengths (Lukashin and Georgopoulos 1994). A generalization of this idea would posit the existence of a very large number of specific networks, one for each skill, a possible but impractical suggestion. At the other extreme, one and the same network could generate different motor behaviors by a continuous modulation of the connections in a single network (Harris-Warrick and Marder 1991). In this study we entertained an intermediate hypothesis, namely that learned motor skills are subserved by largely overlapping

networks with fixed connection strengths. According to this idea, the performance of a learned motor skill involves a network with two kinds of units: (i) general purpose, "core" units that are common to, and, therefore, engaged with, all movements and skills, and (ii) very specialized units that are dedicated to, and, therefore, engaged with, *only* the particular set of movement trajectories comprising a motor skill. Visually guided pointing (1-7) or tracing (8) movements could be generated by the core network, whereas learned skilled movements could be generated by the concomitant activation of both the core and the specialized units. This would be a distributed mechanism by which great specificity could be achieved with a minimum of dedicated neural resources.

Model

We tested the hypothesis above by using massively interconnected neural networks modeled according to the results of experimental studies (see Georgopoulos et al. 1993); namely (i) the units of the network were assigned preferred directions, (ii) the time-varying, dynamically evolving outcome of the network operation was calculated as the sum of the vectorial contribution of these units [i.e. network population vector], and (iii) such population vectors were added successively tip-to-tail to create a "neural" trajectory (Georgopoulos et al. 1988). Specifically, if $\boldsymbol{C}_i$ is the unit preferred direction vector for the i^{th} cell, then the neuronal population vector $\boldsymbol{P}$ is defined as the weighted sum of these vectors:

$$P(t) = \sum_i V_i(t)\, C_i \qquad (1)$$

where the weight $V_i(t)$ is the activity (frequency of discharge) of the i^{th} unit at time bin t. In accordance with experimental data (Georgopoulos et al. 1993) the preferred directions were randomly and uniformly distributed in space. A neural trajectory was obtained by attaching successive population vectors:

$$R(t_k) = \sum_{n=1}^{k} P(t_n) \qquad (2)$$

where the radius-vector $\boldsymbol{R}(t_k)$ defines the point at the neural-vector trajectory taken at time bin t_k.

To calculate a neural trajectory a standard set of resistance-capacitance equations governing the interactions between units and their dynamic evolution was used (Hopfield and Tank 1986) . The time-dependent output activity of the i^{th} unit $V_i(t)$ was calculated as $V_i(t) = \tanh[u_i(t)]$, where the variable $u_i(t)$ represents the internal state (for instance, soma membrane potential) of the unit. The dynamic evolution of the pattern of activity of N interconnected units was governed by the following system of equations:

$$\tau \frac{d u_i}{dt} = - u_i(t) + \sum_{j=1}^{N} w_{ij} V_j(t) + \cos(\theta - \alpha_i) \qquad (3)$$

where $i = 1,..., N$; argument t is shown for values which depend on time; τ is a characteristic time constant; w_{ij} is the connection strength between units ($j \rightarrow i$). The third term on the right hand side of Eq. 3 serves to assign a preferred direction to the i^{th} unit via extrinsic input. The angle θ corresponds to an externally given initial direction, and the angle α_i is regarded as the preferred direction of the i^{th} unit. In the two-dimensional case the angle α_i uniquely defines the unit preferred direction vector $\boldsymbol{C}_i$. In routine calculations, Eq. 3 were solved as an initial value problem using fourth order Runge-Kutta formula with automatic control of the step size during the integration.

The network was trained to generate four different two-dimensional complex trajectories: a clockwise circle, an orthogonal bend, a counterclockwise circle and a sinusoid. Each of these trajectories was generated by a network that comprised a general-purpose, core part (large ovoid) *plus* a special-purpose set of units specific for the particular trajectory (one of the small ovoids). The core part is common to, and shared by, all four networks, and is, therefore, activated regardless of the shape of the trajectory: the particular shape of a trajectory depends on the specific set of units activated, together with the core units, while the remaining trajectory-specific sets are inactive. The connection strengths among the units of the core part are *fixed* and remain the same for all trajectories. On the other hand, the connection strengths between the core units and the trajectory-specific units, and those among the specific units themselves, are allowed to change during training ("*variable*" connection strengths) of the network.

Training procedure

To train the network to generate desired trajectories the *variable* synaptic weights were adjusted by means of the simulated annealing algorithm (Kirkpatrick et al. 1983). Specifically, the simulated annealing procedure was used to minimize the root-mean-square (RMS) error between the desired trajectory shape and that generated by the network:

$$F = \left(\frac{1}{K} \sum_{k=1}^{K} \left| \mathrm{R_d}(t_k) - \mathrm{R_a}(t_k) \right|^2 \right)^{1/2}$$

where the radius-vectors $\boldsymbol{R}_d(t_k)$ and $\boldsymbol{R}_a(t_k)$ show the corresponding points at the desired trajectory and at actual trajectory generated by the network taken at time t_k, and $\boldsymbol{R}_a(t_0) = \boldsymbol{R}_d(t_0)$. In routine calculations we considered 200 points ($K = 200$ in Eq.**4**). Each step of the simulated annealing procedure included a random change of one of the variable synaptic weights followed by an entire recalculation of the trajectory generated by the network. The new value of the synaptic weight was accepted not only for changes that lowered the RMS error, but also for changes that raised it. The probability of the latter event was chosen such that the system eventually obeyed the Boltzmann distribution at a given "temperature", if the RMS error is treated as the "energy" of the system. The temperature was decreased according to a cooling schedule $T_{n+1} = \beta T_n$, where

T_n was the temperature at the n^{th} step and the value 1 - β was varied within the interval from $5x10^{-4}$ to 10^{-5}. Each trial of the training procedure was repeated with different cooling schedules (different values of the parameter 1 - β) to avoid the local minima problem. Generally, if the cooling is sufficiently slow for equilibrium to be established at each temperature, the global minimum, i.e. $F = 0$, can be reached in the limit of zero temperature. We checked the robustness of the results with respect to different series of random numbers used during the realization of the simulated annealing procedure. The amount of time required to train the network depended on the number of units in the simulation, on the trajectory used, and on the particular set of connection weights among the core units. For example, the computer time required on a single YMP C-90 processor ranged from 1.5 to 7.3 CPU hours for each trial using 100 units and the clockwise circular trajectory.

Results of simulations and discussion

Given the overlapping design of the networks, we sought to determine the minimal number of trajectory-specific units needed to generate a particular trajectory. Consider a core network consisting of N_c units. We first assigned and *fixed* the synaptic weights between the units of the core part. These synaptic weights were assigned randomly by the relation

$$w_{ij} = \gamma_{ij} + 0.1\left(1 - \frac{2}{\pi}\arccos(C_i C_j)\right)$$

where γ_{ij} was a random number uniformly distributed on the interval [-0.5, 0.5]. The second term on the right hand side of the Eq. 5 was introduced to provide a negative correlation between synaptic weights and the difference between preferred directions of the connected units. This type of correlation between the synaptic weights and properties of directionally tuned units was observed in experimental (Georgopoulos et al. 1993) and modeling studies (Lukashin and Georgopoulos 1994). Then a trajectory-specific part with a given number of units (n = 1,2,3..) was added and the *variable* synaptic weights were adjusted (see above) until the network subset (i.e. core plus specific units) generated the desired trajectory, or until training failure was evident. We considered the training procedure successful if the resulting network was able to generate trajectory which provided the value of the RMS error (Eq. 4) equal to or less than unity. If this was not achieved after $3x10^5$ steps of the simulated annealing procedure, the training was considered unsuccessful. We did not suppose any specificity of the values of variable synaptic weights in comparison with the weights of connections between the core units. During the simulated annealing procedure a new probe value for variable synaptic weight was randomly selected in accordance with Eq. 4. This means that the probe values for variable synaptic weights obeyed the same distribution function as the fixed synaptic weights for connections among the core units.

The value of n just sufficient for successful training was considered to be the minimal sufficient number of trajectory-specific units, n_s, for this trial; this number varied somewhat from trial to trial. For a given number of units N_c in the core part, the procedure above was repeated ten times using different but fixed synaptic weights for connections among the core units. This was carried out for each type of trajectory and for N_c values ranging from 25 to 205.

The number of trajectory-specific units sufficient to generate a particular trajectory was small: for 100 core units, 2-5 trajectory-specific units were sufficient. It is noteworthy that this finding is independent of the particular shape of a trajectory. Moreover, the ratio of trajectory-specific units over the number of core units (n_s/N_c) decreased as the number of core units increased. Although these results cannot be directly extrapolated to very large networks, larger simulations could yield either no improvement in accuracy (saturation) or further decreases in trajectory error. In the latter case the fraction of the trajectory-specific units, relative to the number of core units, could be even less than our estimate of 2-5%.

Thus, in the framework of our model the larger core part of the network does not carry any information about possible movements in the static state because the weights of connections between the core units are the same for all trajectories. All information about the movements is stored in the weights of connections between the core part and the specialized units, and between specialized units themselves. However, once the dynamics gets started by activation of one of the specialized set, the core part reveals specific dynamical behavior for a particular trajectory, due to the driven forces from the specialized units. Therefore, during the dynamics the core part does discriminate different tasks. Note, that the core part also actively influences the dynamics through the feedback connections to the specialized units. The roles played by the core part and by specialized parts are the following. Since the number of specialized units are negligibly small in comparison with the size of the core part, the total output of the whole network is almost entirely provided by the dynamical behavior of the core network which can translate the information to the lower levels of the central nervous system. The role of the small specialized parts is to receive information about the beginning of the movement and to drive the dynamical behavior of the whole network.

Recent neurophysiological studies (e.g. Ashe et al. 1994) have shown that a small percent (1-10%) of cells recorded during performance of learned movements from memory are very specific to a particular trajectory, whereas a relatively large number of cells are engaged during both simple pointing movements and during performance of the specialized movements. These observations are in close quantitative agreement with the results of the present study; indeed, the experimental results can be regarded as reflecting the limit of the theoretical results obtained in this study. In the brain, specialized networks could be activated by various cortical and subcortical structures including the cerebellum and basal ganglia. Finally, the architecture of overlapping, massively interconnected networks with a minimum of specialized units could be useful to other applications requiring the production of very specific outcomes: this architecture is efficient and effective, for it maximizes the specificity that can be obtained while minimizing the number of specific units and allowing for a common core to be shared by different applications.

2. Development of a model of interactions between the cortical and the spinal networks dealing with generating time-varying motoneuronal outputs for movements in space (publications 7-8).

These studies comprised (A) development of a "spinal-type" network processing force production, and (B) modeling of the interactions between motor cortical and spinal networks.

2.A. A spinal-type network processing force production

Abstract

We have developed a model that simulates possible mechanisms by which supraspinal neuronal signals coding forces could converge in the spinal cord and provide an ongoing integrated signal to the motoneuronal pools whose activation results in the exertion of force. The model consists of a three-layered neural network connected to a two-joint-six-muscle model of the arm. The network layers represent supraspinal populations, spinal cord interneurons, and motoneuronal pools. We propose an approach to train the network so that, after the synaptic connections between the layers are adjusted, the performance of the model is consistent with experimental data obtained on different organisms using different experimental paradigms: the stiffness characteristics of human arm; the structure of force fields generated by the stimulation of the frog's spinal cord; and a correlation between motor cortical activity and force exerted by monkey against an immovable object. The model predicts a specific pattern of connections between supraspinal populations coding forces and spinal cord interneurons: the weight of connection should be correlated with directional preference of interconnected units. Finally, our simulations demonstrate that the force generated by the sum of neural signals can be nearly equal to the vector sum of forces generated by each signal independently, in spite of the complex nonlinearities intervening between supraspinal commands and forces exerted by the arm in response to these commands.

Introduction

Recordings of neuronal activity in the motor cortex of behaving animals have shown that the direction and overall trajectory of arm movements are markedly related to the activity of motor cortical cells (Georgopoulos et al. 1982; Georgopoulos et al. 1986; Kalaska et al. 1989; Caminiti et al. 1990; Hocherman and Wise 1991; Georgopoulos et al. 1993; Schwartz 1994). These observations have been extended to the study of forces exerted by the arm against an immovable object (Georgopoulos et al. 1992). A monkey was trained to exert forces on an isometric handle in the presence of a constant force bias. First the monkey was required to exert a postural (static) force $\boldsymbol{P}$, which compensated a given bias force $\boldsymbol{B}$. After a holding period, a cue instructed the monkey to exert a force $\boldsymbol{S}$ so that the net force acting on the handle (i.e., the force exerted by the monkey $\boldsymbol{S}$ *plus* the bias force applied to the handle $\boldsymbol{B}$) was in a visually specified direction $\boldsymbol{N}$.

Note, that the net force is equivalent to the incremental (dynamic) component ***I*** of the force exerted by the subject: ***I=S*B*P=S+B=N***. Eight net force directions and eight bias force directions were employed. Two principal findings were reported: (i) the activity of single cells showed approximately the same directional tuning properties when the arm exerts a force without moving as when it moves through space (Georgopoulos et al. 1993), and (ii) as a population, the activity of cells reflected the direction of the incremental force ***I*** and not the actual force ***S*** exerted by the subject. Accordingly, it was hypothesized (Georgopoulos et al. 1992; Georgopoulos 1994) that the postural and incremental signals are controlled by different neural systems, and that these signals would converge in the spinal cord and produce a resulting integrated signal to the motoneuronal pools.

The hypothesis concerning an integration of separate force signals implies a "linear summation rule": the postural signal, which generates the force ***P***, and the incremental signal, which generates the force ***I***, should converge at the level of spinal cord in such a way that the integrated signal would generate the force ***S*** that is equal to the vector sum ***P+I***. Only in this case the net force acting on the handle (***S+B***) will be equal to the desired net force ***N***. Although an appropriate summation of neuronal *signals* is conceivable (Redish and Touretzky 1994), the linear summation of *forces* seems unlikely, due to the complex nonlinearities that characterize the mechanical properties of limbs, and the interactions both among neurons and between neurons and muscles (Bizzi et al. 1991; Kalaska and Crammond 1992). However, recent evidence derived by focal microstimulation of the frog's spinal cord (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994) has revealed that the simultaneous activation of two distinct spinal sites leads to the vectorial summation of the end-point forces generated by the stimulation of each site separately. Although spinal microstimulation studies have not been performed in primates, it is reasonable to hypothesize a similar plan of spinal organization. Then the synaptic connections between the supraspinal populations and the spinal cord could provide a concomitant activation of a number of the spinal sites associated with different force fields, which are summed in a linear fashion.

The purpose of the present article is to propose and analyze a model that suggests possible mechanisms by which the supraspinal commands could be integrated at the spinal cord level and translated into exertion of a required force. The model consists of a three-layered neural network connected to a two-joint-six-muscle model of the arm. The layers of the network represent supraspinal neuronal populations, spinal cord interneurons, and motoneuronal pools, respectively. The key idea is *to train* the network so that the model reproduces quantitatively experimental data for stiffness characteristics of human arm (Mussa-Ivaldi et al. 1985; Shadmehr et al. 1993; Tsuji et al. 1995), and then *to test* the model by comparing its performance with experimental data obtained from recordings of cell activity in the motor cortex of monkey (Georgopoulos et al. 1992) and by microstimulations of the frog's spinal cord (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994). In particular, the model reconciles the nonlinearities that intervene between supraspinal commands and forces exerted by the arm with the hypothesis concerning the linear summation of forces encoded in activities of potentially separated supraspinal neuronal ensembles.

Model

Neural network model. In the model, the direction and magnitude of incremental force ***I*** is encoded in activities of directionally tuned motor cortical cells (Georgopoulos et al. 1992). Although the supraspinal representation of postural force ***P*** is less known (see, however, Kalaska et al. 1989; Wise 1993; Georgopoulos, 1994), we assume the same distributed representation as for the incremental force. Each population consists of n supraspinal (*SS*) units of m neurons each. All neurons belonging to the same *SS* unit possess the same preferred directions $\boldsymbol{C}_i$ (i=1,...,n) with cosine-like tuning function (see Equation 1 below), and the preferred directions $\boldsymbol{C}_i$ are uniformly distributed in 2-D space (Georgopoulos et al. 1993; Georgopoulos 1994). Therefore, if the activity of supraspinal population represents a force signal ***F*** (***F***=***I*** or ***P***), then the activity of the i-th *SS* unit $V_i^{SS}(\boldsymbol{F})$ is given by the expression:

$$V_i^{SS}(\mathrm{F}) = \frac{a_F}{2}\left(1+\cos\theta_{FC_i}\right)$$

where coefficient a_F is proportional to the number of cells recruited to represent the magnitude of force ***F*** (i.e., the larger is the magnitude of the encoded force, the more neurons from a given *SS* unit are recruited (Evarts et al. 1983; Redish and Touretzky, 1994)), and θ_{FC} is the angle between the direction of force ***F*** and the unit's preferred direction ***C***.

All units from both supraspinal populations are connected to the four units at the *IN* layer representing the level of spinal cord interneurons. To calculate activities of the *IN* units V_j^{IN} (j=1,...,4) we use the following sigmoid activation function:

$$V_j^{IN} = \frac{1}{2}\left[1+\tanh\left(\mathrm{T_j}+\mathrm{U_j^{SS}}\right)\right]$$

where T_j is a synaptic input furnished by sources other than the populations coding forces. These signals provide an initial pattern of activity, needed to establish an initial position of the arm (see Section 3 below), before the commands coding forces ***P*** and ***I*** reach the *IN* layer. The synaptic input U_j^{SS} generated by supraspinal force signals is given by the sum:

$$U_j^{SS} = \sum_{i=1}^{n} w_{ji}\left[V_i^{SS}(\mathrm{P})+\mathrm{V_i^{SS}(I)}\right]$$

where w_{ji} is the weight of connection between the i-th unit from the population coding force ***P*** or ***I*** and the j-th unit belonging to the *IN* layer (for the sake of simplicity we assume the same

connectivity matrix for both supraspinal populations).

Each of the *IN* units is connected to all six units at the *MN* layer representing the level of motoneuronal pools. Activities of *MN* units V_k^{MN} (k=1,...,6) are calculated using the relation:

$$V_k^{MN} = \frac{1}{2}\left[1 + \tanh\left(U_k^{IN}\right)\right]$$

where U_k^{IN} is a synaptic input generated by *IN* units:

$$U_k^{IN} = \sum_{j=1}^{4} z_{kj}\, V_j^{IN}$$

where z_{kj} is the weight of connection between the j-th unit from the *IN* layer and the k-th unit from the *MN* layer.

Model of the arm. We use a planar two-joint-six-muscle model utilized in (Hogan 1985; Flash 1987; Katayama and Kawato 1993). The arm is modeled by two rigid segments ("upper arm " and "forearm") of equal length. The upper arm is attached proximally to an immovable "clavicle" via the shoulder joint and distally to the forearm via the elbow joint. Both single- and double-joint muscles are included. One end of both flexor and extensor single-joint muscles controlling the shoulder joint is attached to the clavicle at a distance b from the shoulder joint (flexor and extensor are attached at different sides of the joint). The other ends of these muscles are attached to the upper arm segment at a distance L from the shoulder joint. Single-joint muscles controlling the elbow joint are attached to the upper arm segment at the distances b from the elbow joint and to the forearm segment at a distance L from the elbow joint. Two-joint muscles are attached at distances b from each joint. Note, that the muscle attachment implies that the moment arms of muscles depend upon the joint angles. Below we assume that the distance between the shoulder and elbow joints is equal to L, and use the limit $b<<L$; specifically, we set b=0.01 m, L=0.33 m.

All muscles are modeled by nonlinear springs with the following length-tension relationship (Feldman 1966; Shadmehr and Arbib 1992):

$$f_k = \alpha\,\{\exp[\beta\,(l_k - l_k^o)] - 1\} \quad (l_k > l_k^o)$$
$$f_k = 0 \qquad\qquad (l_k \le l_k^o)$$

where f_k is a contraction force developed by the k-th muscle, l_k is the actual muscle length and l_k^o is the muscle intrinsic rest length; parameters α and β are constants, and α=10 N, β=100 m^{-1}.

These specific values of parameters α and β were chosen to fit by equation (6) the experimental data of Feldman (1966, as presented in Fig.3C of the paper by Shadmehr and Arbib 1992).

Interactions between neurons and muscles. Each unit from the *MN* layer innervates one muscle and controls the muscle intrinsic rest length l_k° (Feldman 1966; Shadmehr and Arbib 1992). We use the following relation between l_k° and activity V_k^{MN} of motoneuronal unit:

$$l_k^\circ = l^{max} + V_k^{MN} (l^{min} - l^{max})$$

where l^{min} and l^{max} are the minimal and maximal muscle rest length, respectively, and l^{min}=0.26 m, l^{max}=0.30 m. Equation (7) implies that the higher is the activity V_k^{MN}, the shorter is the muscle rest length l_k°.

Equilibrium position and restoring force field. Given a particular set of muscle rest lengths l_k° (k=1,...,6), a corresponding equilibrium configuration of the arm can be calculated as follows. Let a configuration of the arm be defined by a pair of shoulder and elbow joint angles (φ_s and φ_e, respectively; $0^\circ \le \varphi_s \le 135^\circ$, $0^\circ \le \varphi_e \le 180^\circ$). Then the set of actual muscle lengths l_k (k=1,...6) is uniquely defined by the geometry of muscles attachment. If muscle rest lengths l_k° and muscle actual lengths l_k are known, the forces produced by muscles can be calculated using (6). Let $(f_1 f_2 f_3 f_4 f_5 f_6)^T$ be the vector of muscle forces (subscripts 1 and 2 refer to the single-joint shoulder flexor and extensor, subscripts 3 and 4 refer to the elbow single joint flexor and extensor, and subscripts 5 and 6 refer to the double-joint flexor and extensor). The transformation between the vector of muscle forces and the vector of net joint torques $(t_s\ t_e)^T$, where t_s and t_e are shoulder and elbow torques, respectively, is given by the matrix of muscle moment arms. For the model described above, this relationship is:

$$\begin{pmatrix} t_s \\ t_e \end{pmatrix} = \begin{pmatrix} -r_s & r_s & 0 & 0 & -r_s & r_s \\ 0 & 0 & -r_e & r_e & -r_e & r_e \end{pmatrix} (f_1 f_2 f_3 f_4 f_5 f_6)^T$$

where $r_s=b\sin\varphi_s$, $r_e=b\sin\varphi_e$. The equilibrium configuration of the arm is defined by the condition that both net joint torques, t_s and t_e, are equal to zero. Consequently, the equilibrium joint angles φ_s^{eq} and φ_e^{eq} can be obtained as the solution of the system of two nonlinear equations (8) under conditions $t_s=0$ and $t_e=0$.

The force exerted by the end-point of the arm is the result of difference between current and equilibrium end-point positions. Generally, each equilibrium position is characterized by a field of restoring forces generated by muscles in response to displacements of end-point from equilibrium position. For any given set of muscle rest lengths, the restoring force field can be calculated as follows. Let a current end-point position be defined by joint angles $?_s$ and $?_e$. Then Equation (8) can be used to calculate the joint torques t_s and t_e (in particular, if the arm configuration is such that $\varphi_s=\varphi_s^{eq}$ and $\varphi_e=\varphi_e^{eq}$, Equation 8 gives $t_s=0$ and $t_e=0$). The transformation between net joint torques and x-y components of restoring end-point force (Q_x and Q_y) is given by the inverse Jacobian matrix:

$$\begin{pmatrix} Q_x \\ Q_y \end{pmatrix} = \frac{1}{L\sin\varphi_e} \begin{pmatrix} \cos(\varphi_s+\varphi_e) & -\cos(\varphi_s+\varphi_e)-\cos\varphi_s \\ \sin(\varphi_s+\varphi_s) & -\sin(\varphi_s+\varphi_e)-\sin\varphi_s \end{pmatrix} \begin{pmatrix} t_s \\ t_e \end{pmatrix}$$

The vector field $\{Q_x(\varphi_s,\varphi_e), Q_y(\varphi_s,\varphi_e)\}$ is the restoring force field associated with the given set of muscle rest lengths.

Performance of the model. All parameters related to the arm construction and elastic properties of muscles will be fixed throughout the rest part of the paper. Since the restoring force field and equilibrium end-point position are uniquely determined by activities of the *MN* units (6-9), the relation between force signals encoded in supraspinal populations (input) and the force exerted by the arm (output) is determined by synaptic connections w_{ji} and z_{kj} between neurons in different layers (Equations 1-5). Therefore, a desired performance of the model can be attained by training of the network, i.e., by an adjustment of synaptic connections.

Training-testing procedure

In the present section of the paper we describe in detail the method used to adjust the synaptic connections. First the synaptic connections z_{kj} between the *IN* and *MN* layers have been adjusted so that any pattern of activity at the *IN* layer produces a restoring force field whose structure is consistent with experimental data obtained for human arm. In particular, each *IN* unit is attributed to a specific point in the workspace, which is the equilibrium end-point position produced by the activation of this unit ("directional preference" of the unit given a reference position in the workspace). Then the synaptic connections w_{ji} between supraspinal populations and the *IN* units have been assigned so that activities of the *SS* units weighted in accordance with their preferred directions $\boldsymbol{C}_i$ are transformed into activities of the *IN* units weighted in accordance

with their directional preferences in the workspace of the arm (connections z_{kj} between the *IN* and *MN* units are kept fixed to retain the structure of force fields). Finally, the overall performance of the model have been tested by independent or simultaneous activations of supraspinal populations.

Connections between the IN and MN units. Forces exerted by individual muscles depend upon the muscle rest lengths (6), which are controlled by activities of the corresponding *MN* units (7). Therefore, activities of different *MN* units should be correlated to produce muscle synergies that ensure desired characteristics of restoring force fields. Since any unit from the *IN* layer is connected to all units at the *MN* layer (4,5), correlated patterns of the MN activity can be provided by a set of "synergetic" synaptic connections between the *IN* and *MN* units. The problem we address is to find a set of connections z_{kj} such that the restoring force fields generated by the model would be similar to the fields measured for human arm (Mussa-Ivaldi et al. 1985; Shadmehr et al. 1993; Tsuji et al. 1995). In these studies, human arm stiffness characteristics have been determined by measuring the restoring forces for displacements from an equilibrium end-point position. The stiffness was represented graphically by an ellipse, characterized by its size, shape, and orientation. The results indicated that the shape and orientation of the stiffness ellipse are strongly dependent on arm configuration in an orderly fashion (these parameters, however, remain invariant among subjects and over time). To adjust the performance of the model to these experimental data we used the following procedure.

Four equilibrium positions of the arm were chosen in the workspace. For each position, we calculated the set of muscle rest lengths l_k° (k=1,...,6) ensuring the size, shape and orientation of the stiffness ellipse in close agreement with these characteristics measured experimentally (Mussa-Ivaldi et al. 1985) for the human arm at a similar location in the workspace. Note, that due to the presence of more muscles than there are joints, different sets of muscle rest lengths may result in the same equilibrium position of the arm. However, it is this redundancy that makes it possible to find a required set of muscle rest lengths imposing the stiffness characteristics as additional conditions. Starting from (8) we have derived explicit relations between muscle rest lengths and the stiffness characteristics of the arm using straightforward algebra, cumbersome as it is (Appendix A).

Each of these equilibrium positions was attributed to one of the *IN* units: namely, for each of four *IN* units (j=1,...,4), six parameters z_{kj} (k=1,...,6) were adjusted so that the maximal activity of the j-th *IN* unit (whereas other units are inactive) generates the attributed equilibrium position.

The resulting connectivity matrix z_{kj} (k=1,...,6; j=1,...,4) was fixed and used during the following testing procedure. Different patterns of *IN* activity were sampled to produce new equilibrium positions, for which stiffness ellipses were calculated. We found that the shape and orientation of ellipses strongly depend on arm configuration, reproducing well two main features of the human arm stiffness (Mussa-Ivaldi et al. 1985; Tsuji et al.,1995): (i) the direction of maximum stiffness at any location is approximately oriented along a radial line joining the hand to the shoulder, and (ii) the stiffness ellipse becomes more anisotropic as the hand approaches distal positions.

Since the stiffness describes the relation between force and displacement vectors only in the vicinity of equilibrium, the performance of the model was further tested for relatively large displacements from equilibrium positions. The structure of restoring force fields is similar to that

measured experimentally (Shadmehr et al. 1993) for the same range of displacements, including a nonlinearity with respect to displacement.

In summary, the use of experimental data for few equilibrium positions as training "examples" makes it possible to find the connectivity matrix z that provides the required synergy of muscles at other locations in the workspace.

Connections between the SS and IN units. The connectivity matrix w transforms a force signal encoded in activities of *SS* units, which are characterized by preferred directions $\boldsymbol{C}_i$ (1), into a signal encoded in activities of *IN* units, which are attributed to specific equilibrium positions in the workspace. Consider a point chosen approximately at the center of the workspace. Let $\boldsymbol{D}_j$ be a unit vector pointed from the center of the workspace to the equilibrium end-point position attributed to the j-th *IN* unit (in a sense, $\boldsymbol{D}_j$ is the preferred direction vector of the j-th *IN* unit). We propose the following expression for the connectivity matrix:

$$w_{ji} = \frac{4}{n} \cos\theta_{\mathrm{D_j C_i}}$$

where θ_{DC} is the angle between vectors $\boldsymbol{D}$ and $\boldsymbol{C}$, and $4/n$ is a normalizing coefficient (n is the number of *SS* units). The idea underlying the use of the above relation is that Equation 10 provides a negative correlation between connection strength w_{ji} and angle between vectors $\boldsymbol{D}_j$ and $\boldsymbol{C}_i$, i.e., the connection strength is correlated with directional preference of connected units. The cosine function (10) and the normalizing coefficient are chosen to obtain activities of *IN* units V_j^{IN} (2) in a simple explicit form. Indeed, substituting (1,3,10) into (2), one has

$$V_j^{IN} = \frac{1}{2}\left[1 + \tanh\left(\mathrm{T_j} + \mathrm{a_P}\ \cos\theta_{\mathrm{P D_j}} + \mathrm{a_I}\ \cos\theta_{\mathrm{I D_j}}\ \right)\right]$$

(to derive (11) we have used the uniformness of distribution of preferred directions $\boldsymbol{C}_i$ (i=1,...,n) and straightforward trigonometric relationships).

In summary, the connectivity matrix w (10) transforms supraspinal signals coding forces $\boldsymbol{P}$ and $\boldsymbol{I}$ (1) into a pattern of activity of the *IN* units (11) in a way that the closer is the direction of force to be exerted (either $\boldsymbol{P}$ or $\boldsymbol{I}$) to the direction of vector $\boldsymbol{D}_j$, the higher is the activity of the j-th *IN* unit.

Transformation of neuronal signal into exertion of force

After the synaptic connections w_{ji} and z_{kj} were adjusted (see Section 3) and fixed, we analyzed the performance of the model as follows.

First coefficients a_P and a_I characterizing the magnitude of force signals were set to zero,

and additional inputs T_j (11) were adjusted to obtain such initial pattern of the *IN* activity that produces the equilibrium end-point position located approximately at the center of the workspace. Using this point as the origin, the preferred direction vectors $\boldsymbol{D}_j$ (j=1,...,4) were defined as unit vectors pointed from the origin to one of four equilibrium positions.

Eight signals coding the postural forces $\boldsymbol{P}$ of equal magnitude (a_P=0.3) and different directions ranging from 0 to 360° were given, and corresponding patterns of the *IN* activity were calculated in the absence of incremental force signal (a_I=0). Each of these patterns produces a new equilibrium end-point position, which differs from the initial position of the arm. Due to this difference, a restoring force appears. If the arm is free to move, then the restoring force would result in a new position of the arm. Otherwise, the restoring force can be referred to the force exerted by the arm against an immovable object measured in the experiment (Georgopoulos et al. 1992). We have calculated end-point forces generated by the eight neuronal signals using (1-11). We found that the model properly transforms neuronal signals of different directions into exertion of force. A difference between directions of force signals and generated forces can be reduced by an additional adjustment of the connectivity matrix w.

To test whether the "vectorial summation rule" (see above) is valid in the framework of the model we calculated restoring end-point forces produced in response to simultaneous activation of both supraspinal populations (i.e., a_P=0.3, a_I=0.3). We found that in all 64 cases the sum of neuronal signals is transformed into the force that is nearly equal to the vector sum of forces generated by each signal separately.

The performance of the model can be interpreted in the light of experimental data reported in (Georgopoulos et al. 1992; see also Section 1 of the present paper for a discussion). To this end, we refer the net force $\boldsymbol{N}$ acting on an immovable handle in the presence of bias force $\boldsymbol{B}$ (Georgopoulos et al. 1992) to the force calculated within the model as the difference $\boldsymbol{S}\mathrm{B}\boldsymbol{P}$, where $\boldsymbol{S}$ is the force generated by the sum of postural and incremental signals, and $\boldsymbol{P}$ is the force generated in response to the postural signal (we suppose that the postural signal $\boldsymbol{P}$ compensates exactly the bias force $\boldsymbol{B}$, i.e., $\boldsymbol{P}$=B$\boldsymbol{B}$). The performance of the model would be consistent with the experimental findings (Georgopoulos et al. 1992) if the direction of "net force" $\boldsymbol{S}\mathrm{B}\boldsymbol{P}$ is close to the direction of incremental component $\boldsymbol{I}$, regardless of the direction of postural force $\boldsymbol{P}$. In other words, the vectorial summation rule $\boldsymbol{S}=\boldsymbol{P}+\boldsymbol{I}$ should be valid. We have calculated the net forces $\boldsymbol{S}\mathrm{B}\boldsymbol{P}$ for eight different directions of incremental signal and eight different directions of postural signal. We found that while the direction of postural force $\boldsymbol{P}$ changes from 0 to 360° within each cluster, the direction of net force $\boldsymbol{S}\mathrm{B}\boldsymbol{P}$ remains almost invariant and close to the direction of incremental component $\boldsymbol{I}$. In fact, this is another interpretation of the vectorial summation rule.

Summation of restoring force fields

Although parameters of the model have been adjusted to reproduce the results of specific experiments performed on human and monkey (see above), it is useful to compare the restoring force fields generated by the model with experiments performed on the spinalized frog (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994). The results obtained by microstimulation of the frog's spinal cord suggested that the neural circuits in the spinal cord are organized in a set of control modules that "store" a few limb postures in the form of convergent force fields acting

on the limb's end-point. Moreover, it was demonstrated (Bizzi et al. 1991; Mussa-Ivaldi et al. 1994) that simultaneous stimulation of two distinct spinal sites results in a field of forces proportional to the vector sum of the fields induced by the independent stimulation of each site. These findings have led to a new concept of the motor control (Bizzi et al. 1991; Mussa-Ivaldi and Giszter 1992) based on the vector combination of a few convergent fields to produce a vast repertoire of motor behavior. Below we demonstrate that the proposed model generates restoring force fields whose properties are in close similarity with those reported in (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994).

Justification of the model. To establish a correspondence between the model and experiment (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994) we used the following approach. The *IN* layer of the model was disconnected from the supraspinal layers, i.e. the model was "spinalized". First of all, we calculated the force field generated under condition that all units at the *IN* layer are inactive. Since the *MN* units are also inactive, the muscle rest lengths in this case are equal to their maximal possible values (7). We refer this field to the "resting" force field measured in the absence of stimulation (Giszter et al. 1993). The stimulation of a particular spinal site in the experiment was referred to the activation of a particular unit at the *IN* layer. The activation of distinct units resulted in different force fields converging to different equilibrium points. We referred these fields to the "total" force fields measured during stimulations of different sites (Bizzi et al. 1991; Giszter et al. 1993). Next, following the experimental procedure described in (Giszter et al. 1993), we calculated the "active" force fields by subtraction the resting field from the total fields. We found that the structure of force fields is similar to that measured experimentally (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994).

Co-activation of distinct sites. Experimental results (Bizzi et al. 1991; Mussa-Ivaldi et al. 1994) suggested that the "vectorial summation rule" is valid for the active fields. We compared the active field generated by the simultaneous activation of two *IN* units to the vector sum of the fields generated by the independent activation of the same units. As it was suggested by Mussa-Ivaldi et al. (1994), to quantify the similarity between the sum and co-activation fields, we calculated the "cosine" of the angle between these two sampled fields, and used for this measure the value of 0.90 as a threshold for similarity (the maximum value of the similarity is equal to 1). There are four units at the *IN* layer and, therefore, there are six different pairs of them. We have found that, for all six pairs, the similarity between the sum and co-activation fields exceeded the threshold value ranging from 0.97 to 0.99.

We extended this analysis comparing the vector sum of fields generated by two random patterns of the *IN* activity (the activity of each unit is a continuous variable ranging from 0 to 1) with the co-activation field generated by superposition of these patterns. We calculated the sum and co-activation fields for 10,000 pairs of random patterns. The similarity between these fields was dependent on the sampled patterns ranging from 0.71 to 0.99. Therefore, the co-activation field generated by superposition of two arbitrary patterns may differ dramatically from the sum of the fields generated by each of these patterns independently (e.g., the value of 0.71 corresponds to the average angle between sample vectors equal to 45 degrees). This result was expected because of the nonlinearity of the model. However, the number of cases in which the similarity was below the threshold value 0.90 comprised less than 15% of the total number of

trials. Averaged over all trials the similarity between the sum and co-activation fields was 0.96 ± 0.04, which is consistent with the average similarity across the entire set of experimental data 0.94 ± 0.05 (Mussa-Ivaldi et al. 1994).

In summary, the force fields have been calculated within the same model that has been adjusted and tested above. None of the parameters has been changed, neither introduced additionally. Nevertheless, these results indicate that basic features of the force fields obtained by the spinal stimulation of the frog's limb (Bizzi et al. 1991; Giszter et al. 1993; Mussa-Ivaldi et al. 1994), such as a convergence of total fields to equilibrium points, typical nonlinear dependence of the force direction and magnitude upon the position in the workspace, and the "vectorial summation rule", are well reproduced within the model.

Conclusions

The complexity of real biological systems controlling motor behaviors is such that no practical models attempt to describe them in full detail. In this paper we focused on a particular aspect of the problem: what are possible mechanisms underlying the *integration* of neuronal commands from different systems to produce a required force. We aimed to develop a model of the "minimal complexity" that would include those factors that are of primarily importance for the problem, making as few assumptions as possible concerning the details left out of the model.

Although the degree of isomorphism between the model and motor physiology should not be overstated (for example, the motoneuron activation function (4) does not contain any feedback component), we believe that the model described in this paper is a reasonable compromise between tractability and realism. Indeed, the structure of the model is really simple: it consists of a standard three-layered feedforward neural network connected to a standard two-joint-six-muscle model of the arm. On the other hand, the model incorporates the following biologically important features: force signals are encoded in the activity of directionally tuned neurons; only a few distinct sites represent the level of spinal cord interneurons; synaptic connections between neural layers result in converging and diverging patterns of influence (in particular, neuronal units from the layer representing spinal cord interneurons make synaptic connections with different pools of motoneurons and activate groups of muscles in a weighted fashion); neuronal units are modelled as elements with nonlinear activation function; the construction of the arm model provides a nonlinear dependence of elastic properties on configuration of the arm, and muscles are modelled by nonlinear springs.

To adjust the performance of the model we used two sets of experimental data. One set (the stiffness characteristics of human arm) was used to train the network, and another set (the correlation between motor cortical activity and the force exerted by monkey, and the structure of restoring force fields generated by stimulation of the frog's spinal cord) was used to test the model performance. We have shown that the performance of the model with a fixed set of parameters is quantitatively consistent with experimental data obtained on three different organisms using different experimental paradigms thus suggesting a universal principle of organization of motor control.

The model predicts a specific pattern of connections between supraspinal populations coding forces and spinal cord interneurons. We have shown that a supraspinal signal can be

properly translated into a required force if strengths of cortical-spinal connections are weighted in accordance with directional preference of connected units (see also Georgopoulos, 1988 and Georgopoulos, 1994, where this type of interactions between cortical and spinal systems was hypothesized). In this paper, the cortical-spinal connectivity matrix is given by an explicit relation (10).

In fact, our investigation originated from experimental findings (Georgopoulos et al. 1992; Mussa-Ivaldi et al., 1994), which raised a question of how essentially nonlinear system could provide a linear summation of forces coding by different neuronal signals. Obviously, a nonlinear system cannot carry out the linear summation *exactly*, merely by definition of what the nonlinearity is. Indeed, our model, which incorporates nonlinearities at all levels (1-11), never performed the exact vectorial summation of forces. However, we have shown that adjustable parameters of the model (synaptic connections) can be chosen in a way that the force generated by the sum of signals is *nearly equal* to the vector sum of forces generated by each signal independently. From this we conclude that approximately linear summation of forces observed in the experiments (Georgopoulos et al. 1992; Mussa-Ivaldi et al. 1994) cannot be a stringent rule, but may reflect a prevalent tendency, which could be provided by patterns of cortical-spinal and spinal interneuron-motoneuronal connections.

2.B. A model of the interactions between motor cortical and spinal networks

Abstract

One problem in motor control concerns the mechanism whereby the central nervous system translates the motor cortical command encoded in cell activity into a coordinated contraction of limb muscles to generate a desired motor output. This problem is closely related to the design of adaptive systems that transform neuronal signals chronically recorded from the motor cortex into the physiologically appropriate motor output of multijoint prosthetic limbs. In this report, we demonstrate how this transformation can be carried out by an artificial neural network using as command signals the actual impulse activity obtained from recordings in the motor cortex of monkeys during the performance of a task that required the exertion of force in different directions. The network receives experimentally measured brain signals and re-codes them into motor actions of a simulated actuator that mimics the primate arm. The actuator responds to the motor cortical commands with surprising fidelity generating forces in close quantitative agreement with those exerted by trained monkeys, in both the temporal and spatial domains. Moreover, we show that the time-varying motor output may be controlled by the impulse activity of as few as 15 motor cortical cells. These results outline a potentially implementable computation scheme that utilizes raw neuronal signals to drive artificial mechanical systems.

Introduction

Neurophysiological studies have shown that motor output (movement or force) produced by a

limb is related to the motor cortical activity and that the population activity of directionally tuned cells within the motor cortex can be used to predict the upcoming motor output under a variety of conditions. However, these experimental results suggest only the cortical representation of the motor command, and do not solve the problem of how this representation could be implemented during motor output. Here, we directly address the question of how the cortical neuronal signals could be used to drive an artificial actuator (e.g., a prosthetic limb) such that the motor output of actuator would correspond to the performance of real limb driven by the central nervous system. This problem is made difficult by the fact that physiologically useful motor output requires the coordinated recruitment of multiple degrees of freedom distributed over artificial limbs. Below we demonstrate how the transformation problem can be solved for a particular example of motor action: the exertion of static isometric force.

Methods

Neuronal signals: The motor cortical activity used in this study as command signals came from single-cell recordings performed previously in our laboratory for other purposes. In that experiment, monkeys were trained to exert 2D forces on an isometric handle so that the force developed over time had to remain in the visually specified direction (the instructed direction) and to increase in magnitude in order to exceed a required threshold. Eight instructed directions uniformly distributed in 2D space were employed. In the present study, we use two data files. The first file consisted of impulse activity of 75 directionally tuned cells recorded in the arm area of the motor cortex. There were 24 spike trains for each cell (8 instructed directions of 3 trials each). The second file consisted of the *x-y* components of the developed force measured each 10 ms for all 1800 trials contained in the first file. Therefore, we have experimentally measured motor cortical commands and resulting motor actions. Our aim was to construct a model that would generate the same motor outputs in response to the same neuronal commands.

Transformation algorithm: We exploit a processing algorithm developed in a previous study. The impulse activity of 15 different cells is presented. These spike trains were recorded in different trials but for the same instructed direction of force (−135° in 2D space). The cortical signal must be transformed into the motor output of a simulated actuator. For example, in order to be consistent with the experimental data, the response of the actuator to the neuronal command should be an end-point force 'exerted' in the direction −135°. The transformation is done by an artificial neural network connected to the actuator. The network receives experimentally measured impulse activity as a time-varying input to the upper layer and transforms it into a time-varying pattern of activity at the output layer as follows. Each neuron at the intermediate layer is connected to all neurons at the upper layer. Intermediate neurons receive the input signals as the sum of spikes from all upper neurons weighted with corresponding strengths of synaptic connections. These inputs are accumulated over the time and transformed into activities of intermediate neurons using the sigmoid activation function. At each instant of time, the collective activity of intermediate layer produces a pattern of activity at the output layer in accordance with the connectivity between these two layers. The output activity of the network is then transformed into analog commands. Due to connections between the output units and the

actuator, a pattern of output activity generates contractions of actuator modeled 'muscles' by means of changing the muscle rest lengths. Let the actuator be at the equilibrium state (equilibrium joint angles) determined by an initial set of muscle rest lengths. Now suppose that because of changes in the network output activity the muscle rest lengths have changed. If the actuator is free to move, then a new equilibrium state would eventually be reached. Otherwise (a possibility, which we explore here), the difference between the previous and new equilibrium states results in an end-point force, which we refer to as the force exerted by the actuator against an immovable object (thick arrow at the end-point). Given a set of new rest lengths, the direction and magnitude of the end-point force can be calculated using straightforward, though cumbersome, algebra. In the framework of this computational scheme, the performance of the model (i.e., the relation between the input cortical signals and the forces exerted) depends mainly on the network connectivity, which must provide a synergistic activation of all muscles to generate the required motor output. We searched the corresponding set of synaptic weights and activation thresholds using the algorithm described in Lukashin et al. (1996).

Results

After the connectivity of the network was found and fixed, we tested the performance of the model across the whole set of experimental data. An important question is the robustness of the computation scheme with respect to the variation in the number of cells generating neuronal signals (N) and with respect to changes in the cell activity from trial to trial. To assess robustness, we adopted an approach that utilized a "bootstrapping" procedure: (i) the cells comprising the population of a given size N were selected from the set of 75 cells (since the uniformness of cell preferred directions throughout the space is of particular importance in reconstructing the directional signal encoded in the population activity, all cells from the original data set were divided into N groups in accordance with their preferred directions so that the i-th group would contain the cells with preferred direction angles ranging from $2\pi(i-1)/N$ to $2\pi i/N$; to comprise the population, one cell from each group was drawn randomly); (ii) for each drawn cell, one of the three trials, for which this cell was recorded from, was chosen randomly; (iii) N spike trains corresponding to the chosen cells and trial numbers were taken from the experimental data file and used as the input activity of the network. This procedure was repeated 1000 times for each of the 8 instructed directions using new sets of selected cells and trial numbers. The size of the population N varied from 4 to 40. To evaluate the performance of the actuator we applied the same criterion as in the experiment (Georgopoulos et al. 1992): the direction of force developed had to be stable and not differ more than ±22.5° from the instructed direction. We have found (data not shown) that the performance improves gradually as the size of population N increases, revealing a tendency for saturation as N approaches 15-20. There was a close similarity between the actuator performance and the motor action of the real arm. We used bootstraps of 1000 randomly selected sets of cells and found that even for this relatively small number of command cells ($N = 15$) the mean directions of forces produced by the actuator were very close to the instructed directions (the circular correlation coefficient $\hat{\rho}_T = 0.988$, $n = 8$ directions). This indicates a high degree robustness of the transformation algorithm.

Discussion

In a sense, the control of isometric force chosen in the present study represents a relatively simple case, if compared with the control of fast movements. For the latter tasks, the problem can be additionally complicated by the necessity of compensating for the dynamic forces (inertia, Coriolis forces, and so on) acting on the limb. In our case, there is no motion and, therefore, there is no need to allow for the dynamic forces. Here, we use a computational model of motor control that has been developed previously (Lukashin et al. 1996) and that brings together a number of experimental and theoretical observations on neuronal activities in the motor cortex (Georgopoulos et al. 1993) and on the mechanics of multijoint limb control (Mussa-Ivaldi et al. 1985, Bizzi et al. 1991, Tsuji et al. 1995, Bizzi et al. 1995). In our previous work (Lukashin et al. 1996) we concentrated on the mechanisms underlying the integration of neuronal commands from different sources, and the cortical activity was modeled by artificial idealized signals. The main point of the present report is that we do not employ the artificial signals. Instead, we deal with raw experimental data[8] without any filtering, approximation or pre-processing.

Our computation scheme successfully decodes these signals, and the time-varying forces developed by the actuator are very similar to those developed by the monkey arm. Following an initial period of time, which lasts 100-200 ms, the direction of force exerted by the actuator stabilizes, and the magnitude of force increases. The stabilized direction of force is close to the instructed direction, for which the cortical activity was recorded. This was also observed for the remaining 4 instructed directions for this particular ensemble of cells and for other ensembles of cells ($N \geq 15$) and trial numbers that were selected by the bootstrapping procedure as described in the previous section. It should be noted that different patterns of cortical activity were processed by the network with a fixed set of adaptive parameters (synaptic weights and activation thresholds).

To evaluate the performance of the model, we used neuronal activity collected from different repeated trials, and most of the cells were not recorded simultaneously. It means that spike trains of different cells were not correlated with each other. For real time applications of the transformation scheme suggested here, the impulse activity of different cells will be recorded simultaneously during an individual trial. In this case, different cells might be correlated, and the correlation could affect the performance of our model. Although we believe that the correlation between spike trains would improve the performance, this is still a conjecture to be tested in the future. Another problem that may arise for real time applications is that some of motor cortical cells can be active in a manner consistent with the incoming motor action during, for example, instructed delays. In such a situation, the motor cortical activity alone might not be sufficient to generate the desired time-course of motor actions, and an additional signal that triggers the system is needed.

Conclusion

If it becomes practical to chronically record motor cortical activity as command signals for electronically driven prostheses or other mechanical systems, then the transformation of such

signals into appropriate motor output would become an important issue. The reliable decoding and transformation of neuronal ensemble activity recorded in behaving animals as demonstrated here suggests that the use of biologically inspired neural networks to transform raw cortical signals into the motor output of a multijoint artificial limb is both feasible and practical.

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